disrupting the OCH1 gene in a methylotrophic yeast strain; a genetically engineered strain of a methylotrophic yeast transformed with at least one of these vectors; a method of reducing glycosylation on proteins produced by the same genetically engineered strain of a methylotrophic yeast; and a kit comprising at least one of these same vectors.

REMARKS

In the Office Action dated July 5, 2006, the Examiner has set forth a requirement for restriction under 35 U.S.C. §121, alleging that the subject matter defined by the claims of the present invention represents the following four separate and distinct inventions:

Group I. Group I, Claims 1, 35-65, 69-73, drawn to a vector capable of expressing an α-1,2-mannosidase; a vector capable of expressing a glycosidase II; a vector for disrupting the OCH1 gene in a methylotrophic yeast strain; a genetically engineered strain of a methylotrophic yeast transformed with at least one of these vectors; a method of reducing glycosylation on proteins produced by the same genetically engineered strain of a methylotrophic yeast; and a kit comprising at least one of these same vectors, classified in class 435, subclasses 320.1; 483.

Group II. Claims 66-68, drawn to a glycoprotein produced by the present invention, classified in class 530, subclass 350.

Group III. Claims 74-88, drawn to a method of producing in methylotrohic yeast, glycoproteins having carbohydrate structures similar to those produced by human cells by introducing into a methylotrophic yeast strain at least one enzyme involved in production into the yeast strain at least one enzyme for production into the yeast strain at least one enzyme for production of $Man_5GlcNAc_2$, classified in class 424,subclass 94.1

Group IV. Claim 89, drawn to a method of producing in methylotrophic yeast, glycoproteins having carbohydrate structures similar to those produced by human cells by providing a methylotrophic yeast strain which does not express at least one enzyme involved in production of high mannose structures, classified in class 435, subclass 254.1.

The Examiner is of the opinion that because the above Groups are allegedly distinct,

separate searches are required and it would be unduly burdensome for the Examiner to search and/or consider the patentability of all the above Groups in a single application.

In addition, the Examiner asserts that if Group I is elected, the present application contains claims directed to the following patentably distinct species of α-1,2-mannosidase in the claimed invention:

a) A single specifically named α-1,2-mannosidase recited in the Markush group of claim 37.[1]

b) A single specifically named promoter recited in the Markush group of claim 40 or claim 46.

c) A single specifically named genetically engineered methylotrophic yeast containing a single vector or a single specific combination of vectors of claims 35, 41 or 47.

d) A single specifically named method requiring transforming the yeast with a single vector or a single specific combination of vectors of claims 35, 41 or 47.

e) A single specifically named kit containing a single vector or a single specific combination of vectors of claims 35, 41 or 47.

In order to be fully responsive to the Examiner's requirement for restriction, Applicants provisionally elect to prosecute the subject matter of Group I, Claims 1, 35-65, 69-73, drawn to a vector capable of expressing an α-1,2-mannosidase; a vector capable of expressing a glucosidase II; a vector for disrupting the OCH1 gene in a methylotrophic yeast strain; a genetically engineered strain of a methylotrophic yeast transformed with at least one of these vectors; a method of reducing glycosylation on proteins produced by the same genetically engineered strain of a methylotrophic yeast; and a kit comprising at least one of these same

[1] The Official Action requires election of species from α-1,2-mannosidase recited in the Markush group of claim 38. In a telephonic communication with the Examiner on August 3, 2006, the Examiner confirmed that the recitation of "Claim 38" should be "Claim 37".

vectors. Applicants also provisionally elect the following species:

a) α-1,2-mannosidase derived from *Trichoderma reesei*.

b) AOX I promoter.

c) A genetically engineered methylotrophic yeast containing a combination of vectors of Claims 35 and 47.

d) A method requiring transforming the yeast with a combination of vectors of Claims 35 and 47.

e) A kit containing a combination of vectors of Claims 35 and 47.

Applicants reserve the right to file one or more divisional applications directed to the non-elected subject matter of Groups II-IV. In addition, Applicants submit that the elected vectors of the present invention use an inducible promoter, e.g., AOX I, or a non-inducible promoter, GAP, under different circumstances. Thus, Applicants respectfully request that the Examiner at least consider both the AOX I promoter and the GAP promoter during prosecution.

Pursuant to 37 C.F.R. §§ 1.111 and 1.143, Applicants hereby traverse the Examiner's requirement for restriction and request reconsideration thereof in view of the following remarks.

An Examiner's authority to require restriction is defined and limited by statute:

> If two or more independent and distinct inventions are claimed in one application, the Commissioner may require the application to be restricted to one of the inventions.

35 U.S.C. § 121, first sentence (emphasis added). The implementing regulations of the Patent and Trademark Office include the mandate that restriction is appropriate only in cases presenting inventions which are both independent and distinct, 37 C.F.R. §§1.141-142. Without a showing of independence and distinctness, a restriction requirement is unauthorized. In the present application, the claims which the Examiner has grouped separately are not "independent and distinct" so as to justify the restriction requirement.

The Examiner alleges that the above Groups are distinct, each from the others. The Examiner acknowledges that Groups I and II are related as process of making and product made. However, the Examiner asserts that Groups I and II are distinct inventions because a glycoprotein of Group II can be made in cultured human cells.

Applicants respectfully submit that Groups I and II are different aspects of a single invention. The method of Group I merely teaches how to make the glycoproteins of Group II and the vector required to express glycoproteins of Group II from a yeast.

The Examiner alleges that Group I and Groups III-IV are distinct methods having different starting materials, and therefore they would require different technical considerations for achieving the desired end-results. The Examiner asserts that none of the methods of Groups III-IV require any one of the vectors in Group I. The Examiner asserts that the method of Group III requires the introduction of at least one enzyme for production of $Man_5GlcNAc_2$, whereas the method of Group IV does not require the use of any vector nor any enzyme, simply providing a methylotrophic yeast strain which does not express at least one enzyme involved in production of high mannose structures. The Examiner alleges that Groups II and III-IV are not related to each other because the glycoprotein of Group II is not required to be produced by any of the methods of Groups III-IV. The Examiner further alleges that Groups III and IV are distinct methods one from the other.

Applicants submit that, although the methods of each group employ different reagents and comprise different steps, these groups are all related to the methods and vectors useful for genetically modifying the glycosylation process in methylotrophic yeast strains to produce glycoproteins with reduced glycosylation. Thus, these groups, by employing one single concept, are related to each other and are not independent. Applicants respectfully submit that these

groups are all different aspects of a single invention.

The courts have recognized that it is in the public interest to permit applicants to claim several aspects of their invention together in one application, as the applicants have done herein. The CCPA has observed:

> We believe the constitutional purpose of the patent system is promoted by encouraging applicants to claim, and therefore to describe in the manner required by 35 U.S.C. §112 all aspects as to what they regard as their invention, regardless of the number of statutory classes involved.

In re Kuehl, 456 F.2d 658, 666, 117 U.S.P.Q. 250, 256 (CCPA 1973). This interest is consistent with the practical reality that a sufficiently detailed disclosure supporting claims to one aspect of an invention customarily is sufficient to support claims in the same application to other aspects of the invention.

The Examiner also states that the inventions have acquired a separate status in the art as evidenced by the separate classification and recognized divergent subject matter and would require independent searches. Thus, the Examiner concludes that restriction for examination purposes is proper.

Reliance on the supposed classification of the groups of claims does not establish independence and distinctness. The classification system has no statutory recognition as evidence of whether inventions are independent and distinct. The classification system is instead an aid in finding and searching for patents.

The classification system is also an unreliable basis for requiring restriction between claims to the various aspects of applicants' unitary invention, because the system exhibits considerable overlap in technical definitions. In particular, the definitions of classes and subclasses in the classification system do not prevent the Examiner from basing patentability

decisions, as to claims assigned to one group, on patent references found in the classes or subclass(es) with which he associated another group of claims.

Furthermore, the classification system is a poor basis for requiring restriction between related aspects of an invention because classifications and definitions change over time. Thus, a classification that might have seemed to support restriction at a given time could change, thereby casting a shadow over the propriety of the restriction requirement later on during the term of the patents issuing from parent and divisional applications. Indeed, classifications seem largely to change in response to considerations of administrative convenience, and often in response to nothing more than growth in the number of patents in a given class or subclass. These considerations have nothing to do with whether the subject matter of patents assigned to different classifications is "independent and distinct" as those terms are used in 35 U.S.C. §121, which fact proves that basing restriction requirements on the classification system is improper.

Applicants respectfully suggest that in view of the continued increase of official fees and the potential limitation of an applicant's financial resources, a practice which arbitrarily imposes restriction requirements may become prohibitive and thereby contravene the constitutional purpose to promote and encourage the progress of science and the useful arts. Moreover, under the regulatory changes as a consequence of the General Agreement on Trade and Tariffs (GATT), applicants are required to conduct simultaneous prosecution, as here, requiring excessive filing costs, or otherwise compromise the term of related patent assets.

It is vital to all applicants that restriction requirements issue only with the proper statutory authorization, because patents issuing on divisional applications which are filed to prosecute claims that the Examiner held to be independent and distinct can be vulnerable to legal challenges alleging double patenting. The third sentence of 35 U.S.C. §121, which states that a

patent issuing on a parent application "shall not be used as a reference" against a divisional application or a patent issued thereon, does not provide comfort to applicants against such allegations. The Court of Appeals for the Federal Circuit has declined to hold that § 121 protects a patentee from an allegation of same-invention double patenting, Studiengesellschaft Kohle GmbH v. Northern Petrochemical Co., 784 F.2d 351, 355, 288 U.S.P.Q. 837, 840 (Fed. Cir. 1986). In Gerber Garment Technology Inc. v. Lectra Systems Inc., 916 F.2d 683, 16 U.S.P.Q. 2d 1436 (Fed. Cir. 1990), the court held that §121 does not insulate a patentee from an allegation of "obviousness-type" double patenting, and in fact affirmed the invalidation on double patenting grounds of a patent that had issued from a divisional application filed following a restriction requirement. Furthermore, it is far from clear that the step of filing a terminal disclaimer is available to resolve a double patenting issue that arises after the issuance of a patent on the divisional application.

All these considerations indicate that the imposition of a restriction requirement with inadequate authority can lead to situations in which an applicant's legitimate patent rights are exposed to uncertainty and even extinguished. Accordingly, to protect a patentee's rights and to serve the public interest in the legitimacy of issued patents, Applicants respectfully urge the Examiner not to require restriction in cases such as the present application wherein various aspects in a unitary invention are claimed.

Finally, Applicants respectfully submit that a determination to make the pending restriction requirement final must evidence the patentable distinctness of all defined four groups, one from the other, as presented by the Examiner.

In view of the foregoing comments, it is respectfully urged that the Examiner reconsider and withdraw the requirement for restriction and provide an action on the merits with respect to all the claims.

Respectfully submitted,

Frank S. DiGiglio
Registration No. 31,346

SCULLY, SCOTT, MURPHY & PRESSER, P. C.
400 Garden City Plaza-STE 300
Garden City, New York 11530
(516) 742-4343

FSD/ZY:ab